Pharmaco-Diagnostics (Rx-Dx) Partnerships Program

A New Proposal to Advance the FDA "Critical Path" and Pharmacogenomics Initiatives

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to the U.S. Food & Drug Administration as a public comment to
Critical Path Initiative—Docket No. 2004-N-0181
Pharmacogenomic Combination Product Co-Development—
Docket No. 2004-N-0279

July 30, 2004

Summary: Proposed herein is a "Pharmaco-Diagnostics (Rx-Dx) Partnerships Program." The Program would provide tangible incentives to pharmaceutical and diagnostics companies to support the development of new genomic and proteomic biomarkers and technologies to better predict and monitor response to new targeted therapies. The Program would (i) offer federal matching funds to joint ventures between pharmaceutical and diagnostic companies using the model of the NIST ATP Program and (ii) extend the exclusivity incentives of the Orphan Drug Act to certain drugs linked with "companion" diagnostics or pharmacogenomic assays.

Background

On March 16, 2004 the FDA released a groundbreaking report entitled *Innovation or Stagnation? Challenge and Opportunity on the Critical Path to New Medical Products* . (www.fda.gov/oc/initiatives/criticalpath) The report provides the FDA's analysis of the "pipeline problem" namely, the recent slowdown, instead of the expected acceleration, in innovative drugs and diagnostics reaching patients. According to the report, despite the explosion of bioscience and genomics research over the past ten years the number of new drug applications submitted to the FDA has actually declined significantly. The problem according the FDA is that "the applied sciences needed for medical product development have not kept pace with the tremendous advances in the basic sciences."

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The report predicted that proteomic biomarkers and pharmacogenomics will help bridge the gap between basic research and the development of new FDA approved drugs and devices. "The emerging techniques of pharmacogenomics and proteomics show great promise for contributing biomarkers to target responders, monitor clinical response, and serve as biomarkers of drug effectiveness." However, according to the report, "much development work" must occur before these diagnostic techniques can be easily and widely used.

The FDA's Critical Path report followed by several months that agency's draft "Pharacogenomics Guidance" that encourages drug developers to conduct pharmacogenomic tests during drug development and clarifies how the FDA will evaluate the resulting data.

Regulatory clarification is necessary but not sufficient to advance these important FDA initiatives. Significant economic barriers will need to be lowered to encourage the development and integration of proteomic biomarkers and pharmacogenomics. These barriers include (i) the lack of capital to support innovative diagnostic development, and (ii) reluctance on the part of pharmaceutical companies to divide or reduce the market for their drugs by linking them to particular genomic profiles.

For the past few years there has been very little investment capital available for companies seeking to develop innovative proteomic and genomic platform technologies, especially since the burst of the "genomics bubble" in 2000. As a recent article in *Business Week* pointed out "a close look at some of the recent deals suggests that VCs are applying the harsh lessons they learned from the hundreds of biotech investments that went sour over the past few years. No longer will they throw money at grandiose promises about potential genomics discoveries or new technology platforms. These days, VCs are demanding blockbuster [drugs] that are likely to hit the market in the next couple of years."

This funding shift is helping to exacerbate an ever widening developmental gap between therapeutic and diagnostic technologies. Pharmaceutical and biotech industry leaders are beginning to voice concern about this gap. "The rate-limiting step [in co-development of diagnostics with drugs] is the industry's ability to develop meaningful diagnostics. Therapies have outpaced diagnostics," noted Genentech President Dr. Susan Desmond-Hellmann.[2] At a high-level NCI Roundtable earlier this year Amgen's head of Oncology complained that "tumors are still classified—and the type and course of therapy determined—using antiquated pathological classification systems despite clear evidence that the biochemical and genetic characteristics of tumors, not their physical appearance, determine whether a given therapy will be successful."[3]

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[2] "A Peek Into Biotech's Future" *Signals—The Online Magazine of Biotechnology* (www.signalsmag.com) June, 2004.

[3] Dr. David Parkinson, VP of Oncology, Amgen. NCI Roundtable, Jan. 2004

The other major economic barrier to widespread pharmacogenomic testing is that many drug companies fear these assays will divide or reduce the market of their approved drugs by narrowing the subset of patients to which the drug may be marketed.

This proposal aims to lower these barriers.

Proposal

It is proposed to create a Pharmaco-Diagnostics (Rx-Dx) Partnerships Program. Its goal would be to provide tangible incentives to pharmaceutical and diagnostics companies to support the development of diagnostics technologies and markers to better predict and monitor response to new targeted therapies. The Program would provide (i) federal matching funds to joint ventures between pharmaceutical and diagnostic companies and (ii) regulatory and exclusivity incentives to drugs and devices jointly approved under this program.

1. Federal Matching Funds

In 1990 the Advanced Technology Program (ATP) (http://www.atp.nist.gov) began to provide cost-shared funding to industry to accelerate the development of high-risk technologies with widespread benefits to the nation. Under ATP a joint venture (two for-profit companies both substantially involved in R&D) can seek government cost sharing of up to 50 percent of yearly project costs for up to 5 years. Typically this amounts to at least $1M / year for 3+ years.

ATP provides an excellent model to encourage and support joint ventures between drug and diagnostic companies. Under the Rx-Dx Program the FDA could partner with NIST (and/or the NIH) and administer a matching program using either existing or new appropriations.[4] For example, under this model a large drug company might provide 40% of funding (along with patient samples from clinical trials) to a small diagnostics company that would cover 10% of the costs to identify markers that correlate with positive response to the drug. The government would cover the remaining 50% of the costs. Intellectual property rights would be negotiated between the companies.[5]

2. Regulatory and Exclusivity Incentives

Congress passed the Orphan Drug Act of 1983 to facilitate the development of drugs for treating diseases that afflict too few people (less than 200,000 persons in the

[4] Funding for such an initiative might fall under the NIH "Roadmap" (http://nihroadmap.nih.gov) that seeks to move more basic discoveries from concept to clinical evaluation.

[5] 20/20 GeneSystems currently has three such agreements in place with pharmaceutical companies (without governmental matching funds.)

U.S.) to motivate drug developers to expend the R&D resources to bring the drug to market. The act offers three incentives to manufacturers of orphan drugs: (i) seven years of marketing exclusivity for the orphan indication, (ii) grants and tax credits to subsidize the cost of testing, and (iii) expedited review by the FDA. See http://www.fda.gov/orphan

Each of these incentives would help overcome the economic barriers associated with co-development of drugs and diagnostics, especially offering marketing exclusivity for drugs indicated for diseases with a particular molecular profile. For example, if a drug designed to treat several common tumors (e.g. prostate and lung cancer) is approved to treat tumors with a particular protein expression pattern or gene mutation (found in fewer than 200,000 patients) that drug could qualify for Orphan status and earn seven years of exclusivity. This would likely be a powerful incentive to motivate many drug companies (including generic drug companies) to actively seek diagnostic partnerships and invest in both platform technology development and biomarker discovery. It would also likely lead to the discovery of new uses of "old" (generic or unapproved) drugs.

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